f) Remarks:

Reconsideration and allowance of the present application in view of the foregoing amendments and accompanying remarks are respectfully requested.

Claims 1-31 were pending in the subject application. Claims 4-8, 10, 12, and 17-31 are withdrawn from consideration. By this Amendment, applicants have canceled claims 13-14, amended claims 1, 9, and 15, and added new claims 32-35. Accordingly, upon entry of this Amendment, original claims 2-3, 11, and 16, amended claims 1, 9, and 15 and new claims 32-35 will be pending and under examination.

Claims 13 and 14 are being canceled without prejudice or disclaimer, and applicants reserve the right to present the subject matter of these claims in this or a subsequent application.

Applicants maintain that amended claims 1, 9, and 15 and new claims 32-35 raise no issue of new matter and are fully supported by the specification as filed.

Support for amended claim 1 may be found *inter alia* in the specification, as originally filed, on page 3, line 17 through page 4, line 2; and on page 13, line 19 through page 14, line 9. The amendment to claim 9 is grammatical. Support for amended claim 15 may be found *inter alia* in the specification, as originally filed, on page 4, lines 3-10. Support for new claim 32 may be found *inter alia* in the specification, as originally filed, on page 3, line 17 through page 4, line 2; and on page 14, line 16 through page 15, line 3. Support for new claim 33 may be found *inter alia* in the specification, as originally filed, on page 3, line 17 through page 4, line 2; and on page 14, line 16 through page 15, line 3. Support for new claim 34 may be found *inter alia* in the specification, as originally filed, on page 3,

line 17 through page 4, line 2; and on page 14, line 16 through page 15, line 3. Support for new claim 35 may be found *inter alia* in the specification, as originally filed, on page 3, line 17 through page 4, line 2; and on page 14, line 16 through page 15, line 3.

Amendments to the claims are being presented in the manner specified in the Notice dated January 31, 2003 entitled "Amendments in a Revised Format Now Permitted."

In the Office Action dated April 11, 2003, the Examiner stated that the Non-Final Rejection in paper no. 8 issued January 30, 2003 has been vacated in view of the supplemental election filed on November 8, 2002.

In the Office Action dated April 11, 2003, the Examiner stated that applicant's election of Group VI (claims 1-3, 9, 11, and 13-16 directed to a nucleic acid encoding MiRP1 and HCN1) in Paper No. 9 is acknowledged. The Examiner stated that because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. §818.03(a)).

The Examiner then stated that claims 4-8, 10, 12, and 17-31 are withdrawn from further consideration pursuant to 37 C.F.R. §1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. The Examiner stated that election was made without traverse in Paper No. 7.

Applicants acknowledge the Examiner's comments mentioned above. However, because generic claims 1 and 15 are believed to be patentable, applicants request reconsideration of the restriction requirement and allowance of the withdrawn claims 4-8, 10, 12, and 17-31.

Drawings

The Examiner stated that new drawings are required in this application because of the objection by the draftperson.

In response, applicants have submitted new Figures (Sheets 1-29) attached hereto as **Exhibit A**.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this objection.

Specification

The Examiner stated that applicant is reminded of the proper language and format for an abstract of the disclosure.

The Examiner stated that the abstract of the disclosure is objected to because the abstract is over 150 words and longer than 15 lines and for the phrase "a A vector" line 18. The Examiner stated that correction is required.

In response, in an attempt to advance prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have amended the abstract. The amended abstract is less than 150 words and less than 15 lines. Moreover, in the amended abstract, applicants have deleted "A" in line 18.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this objection.

Claim Objections

The Examiner stated that claim 14 is objected to because of the following informalities: recites topical administration twice in

the claim. The Examiner stated that "topical administration" is the same as "topical application to the cell". The Examiner suggested removing one of the phrases.

The Examiner also stated that claim 15 is objected to because of the following informalities: misspelling of the word "moyocytes" on line 3.

The Examiner further stated that claim 15 is objected to because of the following informalities: misspelling of the word "form" on line 5 should be **"from** step (a)".

The Examiner then stated that claim 15 is objected to because the steps are numbered (a,b,d) and not numbered in sequential order (a,b,c,d).

The Examiner stated that claim 15 is objected to because of the following informalities: there is an unmatched parenthesis on line 2 step (b) after "(contacting a set of the cardiac myocytes form step (a) with an agent to be assayed for its effects on heart rate;". The Examiner stated that appropriate correction is required.

In response, in an attempt to advance prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claim 14. In addition, applicants have amended claim 15 to recite the correct spellings for "moyocytes" on line 3 and "form" on line 5. Applicants have further amended claim 15 to include the steps in sequential order and to delete the unmatched parenthesis.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw these objections.

Claim Rejections 35 U.S.C. §112, first paragraph

The Examiner stated that claims 1-3, 9, 11, and 13-16 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner stated that the claimed invention embraces performing an assay on a heart that is either *ex vivo* or *in vivo*. The Examiner stated that the assay comprises: a) contacting a cardiac cell of a heart with an effective amount of a compound to cause a sustainable heart rate; b) measuring the heart rate after step a); c) providing the heart with an agent to be assayed for its effect on heart rate; d) measuring the heart rate after step (c); and comparing the difference between step b) and step d), thereby determining whether the agent affects heart rate.

The Examiner then stated that the specification provides working examples that will be briefly discussed herein: Action potential in isolated neonatal and adult rat ventricular myocytes was studied using adenoviral constructs comprising HCN1, HCN2, or HCN4. The Examiner stated that example 1 produces an assay using an adenoviral construct to over-express a nucleic acid encoding HCN2 in rat ventricle cells that produces a pacemaker current comparable to the normal cardiac pacemaker in the sinus node (pages 35-37). The Examiner stated that the assay can be used as a high throughput

rate assay for measuring agents that affect pacemaker current. The Examiner further stated that example 2 is directed to expressing HCN1 or HCN2 individually or with MiRP1 in Xenopus oocytes. The Examiner then stated that both HCN 1 and HCN2 express a small current when injected alone. The Examiner stated that coexpression of HCN 1 or HCN2 with minK results in similar current. The Examiner, however, stated that a much larger current is observed when HCN1 or HCN 2 is coexpressed with MiRP1. The Examiner stated that in view of the In Re Wands factors, the as-filed specification does not allegedly provide sufficient guidance or factual evidence to make and use the claimed methods. The Examiner stated that the specification teaches measuring pacemaker current in isolated cardiac cells using transfection methods comprising contacting the isolated cardiac cells with a nucleic acid encoding HCN1, HCN2, or HCN4 or coexpressing HCN1 or HCN2 with MiRP1. The Examiner, however, stated that the claims read on contacting a cardiac cell in a heart that is either *ex vivo* or *in vivo* and the as-filed specification does not provide sufficient guidance or factual evidence for using a heart in the claimed methods. The Examiner stated that the specification does not allegedly provide a working example of the claimed method. The Examiner stated that the as-filed specification does not allegedly provide sufficient guidance or factual evidence to reasonably correlate using isolated cardiac cells to making and using an assay using a heart that is either *ex vivo* or *in vivo*. The Examiner then stated that one skilled in the art would understand that for the claimed methods to be enabled for using a heart, the heart would have to be fully functional and the specification lacks guidance for what method steps and materials are required for one skilled in the art to use (or maintain) a heart to practice the claimed methods. The Examiner stated that the claims read on an *ex vivo* or an *in vivo* method of measuring the

heart rate and the as-filed specification does not allegedly provide sufficient guidance or factual evidence for measuring the heart rate of an isolated heart in the claimed methods. The Examiner stated that the state of the art is absent (sic) for teaching how to use a heart in an *ex vivo* or *in vivo* assay as set forth in the claims. The Examiner stated that the specification allegedly lacks guidance for what materials and methods are required for how to make and use the claimed assay methods comprising an *ex vivo* heart that display a heart beat. The Examiner stated that it would take one skilled in the art an undue amount of experimentation to practice the claimed methods because the specification does not provide the method steps and materials required for using a heart that is either *ex vivo* or *in vivo* and/or measuring the heart rate of an isolated heart.

The Examiner stated that, as a result, it is not apparent how one skilled in the art determines, without undue experimentation, which of the claimed methods are considered enabled, how is it apparent as to how one skilled in the art, without any undue experimentation, practices any method as contemplated by the claims, particularly given the unpredictability of making and using methods of assaying whether an agent affects heart rate using a heart that is either *ex vivo* or *in vivo* and/or the doubts expressed in the art of record.

The Examiner then stated with respect to claims 13 and 14, it is not allegedly apparent to one skilled in the art how to contact a cardiac cell of a heart that is either *ex vivo* or *in vivo* by co-culturing the heart with a nucleic acid. The Examiner stated that the specification teaches co-culturing cardiac cells with a nucleic

acid *in vitro*. The Examiner, however, stated that the specification and the art of record are absent for any method of co-culturing a heart that is either *ex vivo* or *in vivo* with a nucleic acid. The Examiner stated that the claimed embodiment is not enabled because of the lack of guidance provided by the specification to make and use the claimed methods.

The Examiner stated that, in conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made do not provide sufficient guidance and/or evidence to reasonably enable one skilled in the art to make and use any of the claimed methods. The Examiner stated that given that using a heart that is either *ex vivo* or *in vivo* in an assay was unpredictable at the time the invention was made, and given the lack of sufficient guidance as to practice the methods cited in the claims, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the applicant's disclosure.

In response, in an attempt to advance prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have amended claims 1 and 15 so that claims 1 and 15 embrace performing an assay on a heart that is *in vitro*. Claims 2-3, 9, and 11 either directly or indirectly depend on claim 1. Claims 13-14 have been canceled. Claim 16 is dependent on claim 15.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw these rejections.

Claim Rejections 35 U.S.C. §112, second paragraph

The Examiner stated that claims 13, 14, 15, and 16 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claim 13 recites the limitation "the nucleic acid" in lines 12 and 13 on page 73. The Examiner then stated that there is insufficient basis for this limitation in the claim.

The Examiner stated that claims 13 and 14 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for claiming an improper Markush group. The Examiner stated that the claims recite two distinct groups. The Examiner then stated that one group is directed to routes of administration and the other group is directed products that can be used in a route of administration. The Examiner stated that the members of the group do not possess at least one property in common, which is mainly responsible for their function in the claimed relationship.

The Examiner stated that claim 14 recites the limitation "administration of contacting" in line 14, page 73. The Examiner stated that there is insufficient antecedent basis for this limitation in the claim.

The Examiner stated that claims 15 and 16 recite the limitation "step c)" in line 17, page 74 and that there is insufficient antecedent basis for this limitation in the claim.

The Examiner stated that claims 15 and 16 are rejected under 35

U.S.C. §112, second paragraph, as allegedly being incomplete for omitting essential steps, such omission amounting to a gap between the steps.

In response, in an attempt to advance prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have canceled claims 13-14. In addition, applicants have amended claim 15 to clearly identify step (c). Claim 16 is dependent on claim 15.

Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

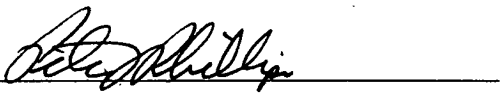
The Examiner stated that claims 1-3, 9, 11, and 13-16 from co-pending application 09/875,392 are the same as the claims 1-3, 9-10, 13-16 from the instant application. The Examiner, however, stated that a statutory double patenting rejection cannot be made at this time since the claims elected in the instant application (claims 1-3, 9, 11, 13-16) are drawn to a different invention than the elected claims (20-31) in `392. The Examiner then stated that should the non-elected claims be re-joined to the elected invention in either application then a statutory double patenting rejection will be made on the claims.

Applicants acknowledge the Examiner's statements mentioned above. In summary, in light of the remarks and amendments made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of rejections set forth in the April 11, 2003 Office Action.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Peter J. Phillips
Registration No. 29,691
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Peter J. Phillips 7/3/03
Reg. No. 29,691 Date